

		A	B
SKD3	EEHPLV-FLFLGSSGIGKTELAKQTAKYMHDAKKGFIRLDMSSEFQERHEYAKFISGPPGYIGHEEGQQ-LTKKLKGCPNAVVLFDEVDKAHPDVLTIMLQLFDEGR...		
HSP-101	PQQPTGSFLFLGPTGVGKTELAKALAEQLF-DNEQLVRIDMSEYWEQHSYSRLLGAPPGYVGHHEEGQQ-LTEAVRRPYSWVLFDEVKEAHTSVFNTLLQVLDDGRL...		
TorsinA	PKKPLTLSL-HGWTGTGKNFVSKIIAENIYEGLN-----SDYVHLFVATLHFPHASNITLYKDALQLWIRGNVSACARSIFIDEMDKMHAGLI DAIKPFLD----		
TorsinB	PKKPLTLSL-HGWTGTGKNFVSKIIAENIYEGLN-----SNFVHLFVSTLHFPEHQKTKLYQDQLQKWIRGNVSACANSVFIDEMDKLHPGII DAIKPFLD----		
TorpCel	PRKPLVLSF-HGYTGSGKNAVEIIIAANNTRFLGLR-----STFVQHIVATNDFPDKNKLEEYQVELRNRIITTVQKCQRSIFIDEADKLPEQQLGAIKPFLD----		
Torpi	PSKPLVLSL-HGWTGTGKSYVSSLAAQLFRDGLR-----SPHVHFSPIIHFPHSRTEQYKRELKSWVGQNLTACERSLFLFDEMDKLPPGLEMVLPQPFLG----		
Torp2	-----AAALHQTLFI DAEAKLHPGLLEVLGPHLER-----		
		SN	IV
SKD3	TDGKCKTIDCKDAIFIMTSNVAASDEIAQHALQLRQEALEMSRNRIAENLGDYQMSDKITISKNFKENVIRPILKAHFRRDEFGLRINEIVYFLPFCHSELIQLVNKEL		
HSP-101	TDGQGRTVDFRNTVIMTSNLGAELLS-GLSGKC-TMQWARDR-----VMQEVRQQ-FRPPELLNRLEDIVWFDPLSHDQLRKVARLQM		
TorsinA	YYDLVGGSYQKAMIFILSNAGAERITDVALDFW-----RSGKREDIKLKDIEHALSVSFNNK--NSGFWHSSLIDRNLIDYFVPELPLEYKHLKMCIRVEM		
TorsinB	YYEQUVGGSYXKAIFIFLSNAGGDILITKITALDFW-----RAGRREDIQLKDIEPVLSVGFFNNK--HSGLWHSGLI DKNLIDYFIPFLPLEYRHVKMCVRAEM		
TorpCel	YYSTISGVDFRRSIFILLSNKGGEARIIKEQY-----ESGPYPREQRLAFTERELMNFSYNEK---GGLQMSSELISNHLIDHYPFLPLQREHVRSVGAYL		
Torpi	PSWWVYGTNYRKAIFIFI SNAGGEQINQVALEAW-----RTNRDREISLQVEPVISRAYMDNP--QHGFWRSGIMEEHILLDAWVPFLPLQRHHVRCVLNEL		
Torp2	RAPEXXGLSLXWTIFLFSNLRGDIINEVVLKLL-----KAGWSREEITMEHLEPHLQAEIVDDH--RQWLWHSRLVKENLIDYFIPFLPLEYRHVRLCARDAF		

FIG. 4C

FIG. 5B

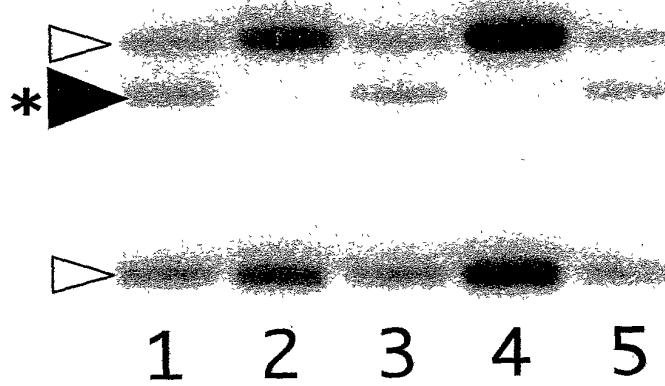


FIG. 5C

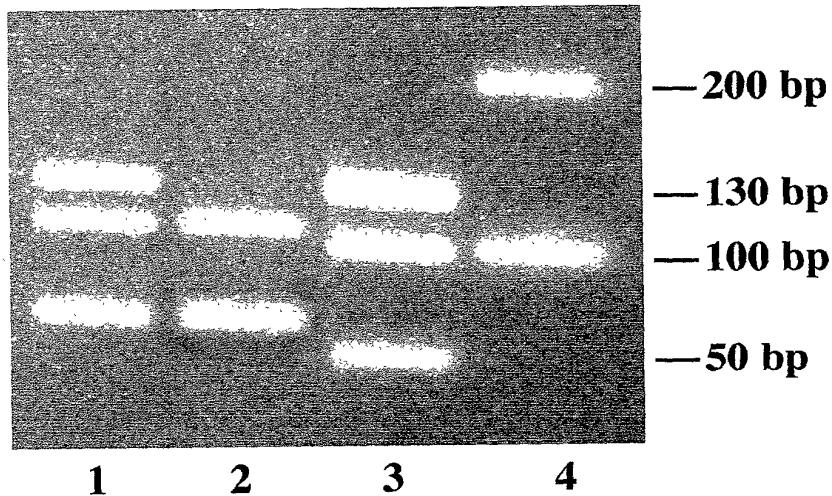
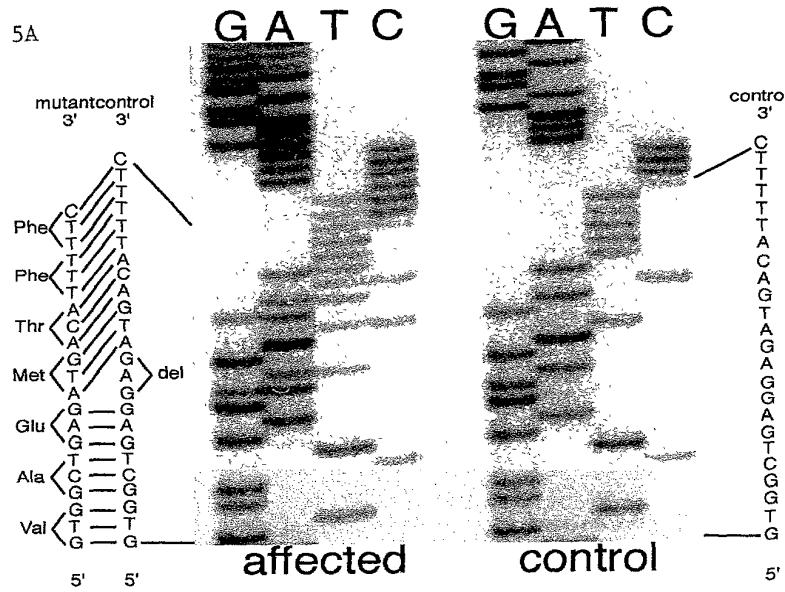


FIG. 5A



Docket No.: 0838.1001-009  
"Torsin, Torsin-Related Genes and M  
Inventors: Laurie J. Ozelius *et al.*

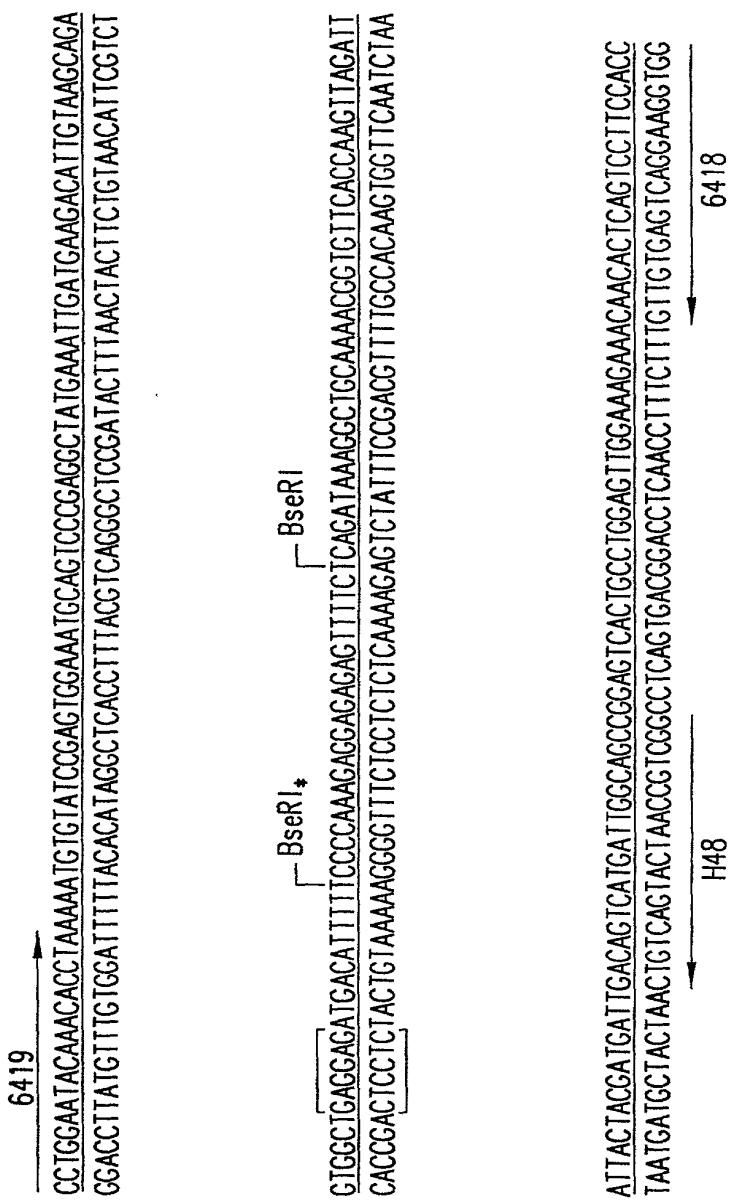


FIG. 5D

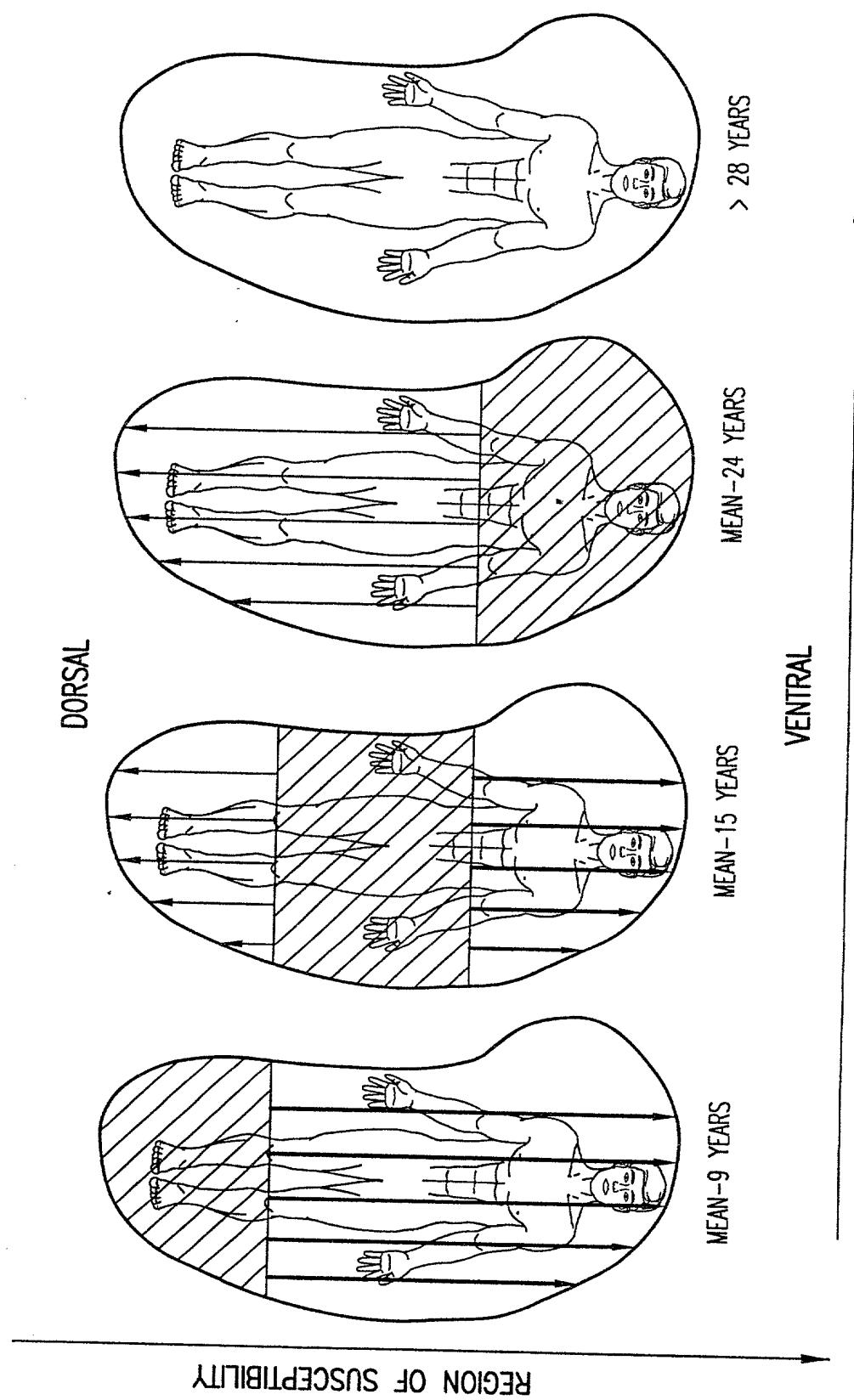


FIG. 6

Docket No.: 0838.1001-009  
"Torsin, Torsin-Related Genes and Methods..."  
Inventors: Laurie J. Ozelius *et al.*

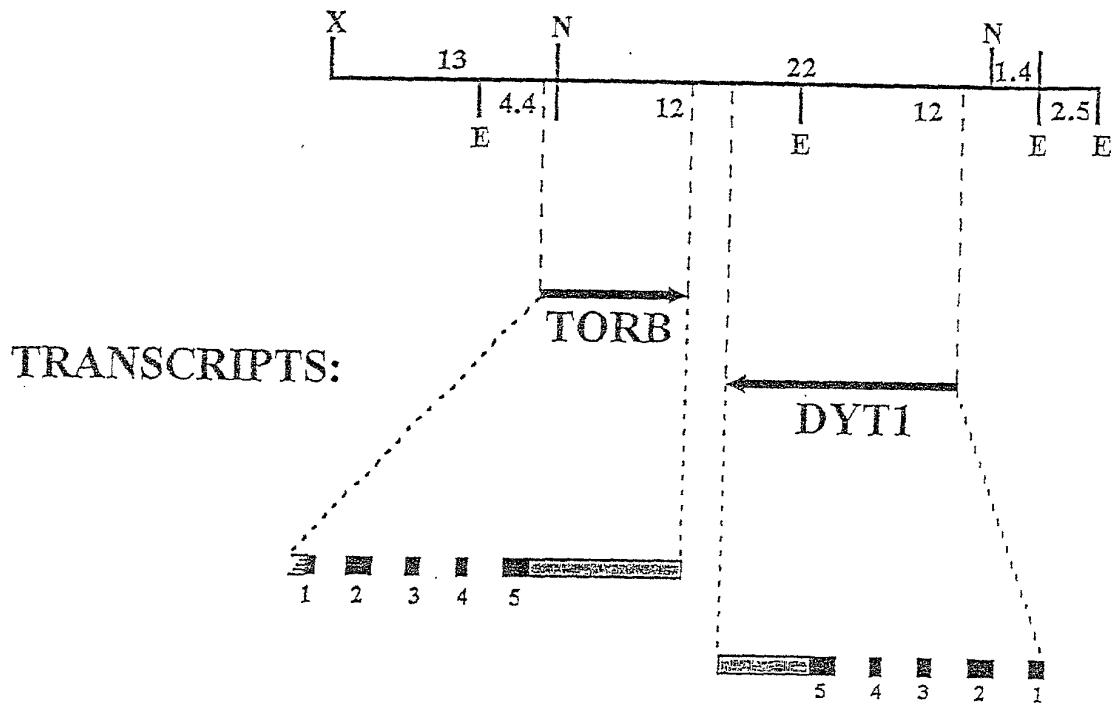


FIG. 7

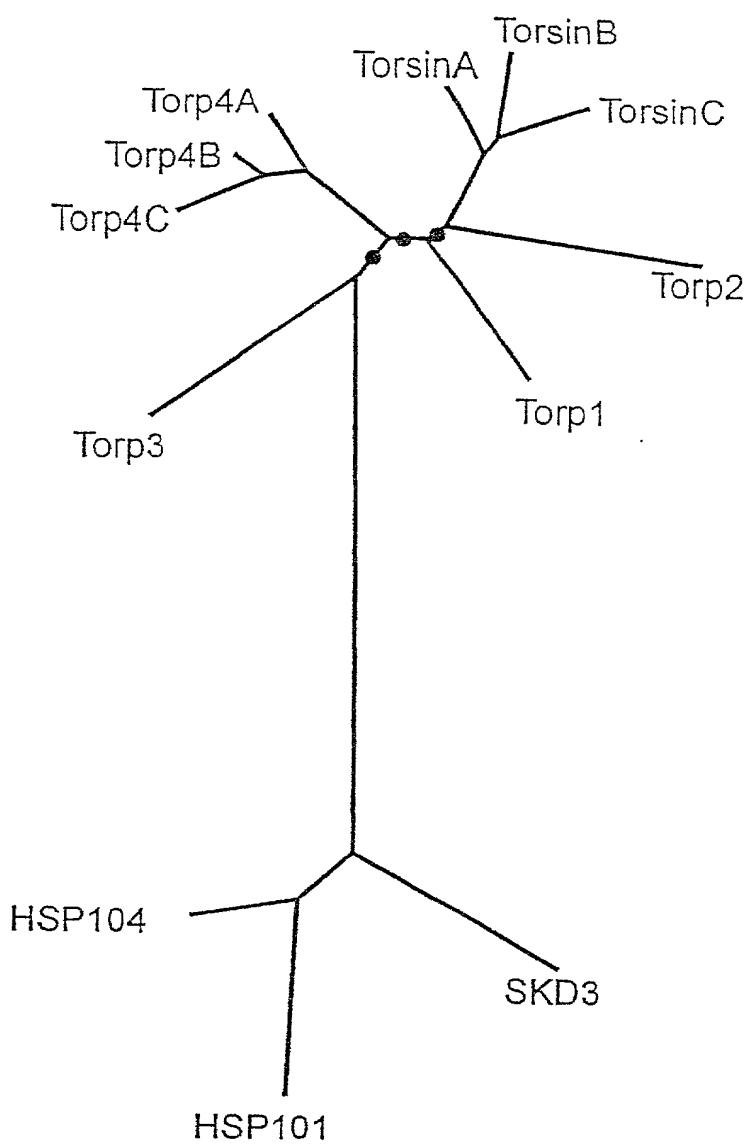


FIG. 8

FIG. 9A

DYTII						
Exon	Size (bp)	3'end of exon	5' splice site (SEQ ID NO)	Intron (kb) <sup>a</sup>	3' splice site (SEQ ID NO)	5' end of exon (SEQ ID NO)
1	178	...CGG GAG R E A	GTAAGGTGG... (67)	1.2	...TCCTTCCCAG (71)	CA CTG CAG AAG... (75)
2	266	...TTG TAC AAG L Y K	GCAAGGATGG... (68)	1.5	...TTAAATTCAAG (72)	L G K
3	176	...TTCTCTCAG F L S	GTAAGGTCAG... (69)	0.097	...TGTTTGCAG (73)	D Q L
4	128	...AAG AAC AG K N S	GTGAGTAGGG... (70)	4	...TTCTTCCCAG (74)	CAAT GCT GGA... (76)
5	251	...GAT GAT TGA D D *			T GGCTTC TGG... (77)	N A G

FIG. 9B

TORB						
Exon	Size (bp)	3'end of exon	5' splice site (SEQ ID NO)	Intron (kb) <sup>a</sup>	3' splice site (SEQ ID NO)	5' end of exon (SEQ ID NO)
1	n.d.	...GCT TCG G A S A		n.d.	...GTTCTTGCAG (81)	CT CTC AAG CTG... (85)
2	266	...CTG TAC CAG L Y Q	GCAAGAGAAC... (78)	3	...GTTGGTCCAG (82)	L K L
3	176	...TTCTCTCAG F L S	GTCAGGGGA... (79)	1.8	...GCAAACCTCAAG (83)	D Q L
4	128	...AAA CAC AG K H S	GTGAGTCCAC... (80)	.31	...TGTTCTGCAG (84)	CAAT GCA GGC... (86)
5	242	...TTC CAC TGA F H *			T GGC CTG TGG... (87)	N A G

\*Sizes of introns were approximated by gel resolution of PCR products

Docket No.: 0838.1001-009  
 "Torsin, Torsin-Related Genes and Methods..."  
 Inventors: Laurie J. Ozelius *et al.*

Type	Number of Individuals	Age of onset yrs	Site of onset <sup>a</sup> (no.)	Sites involved (no.)
<b>Early onset:</b>				
AJ	5	6, 8, 10, 19	A(4), ANL(1)	A(7), N(3), T(1), L(2)
NJ	12	3, 6(2), 8, 9, 10, 11, 13, 14(2), 16, 18	A(9), AU(1)	A(20), G(9),
<b>Potential homozygosity:</b>				
A.J <sup>b</sup>	5	4, 6, 7, 26, 35	L(4), M(1)	L(4), M(1), N(2), P(1),
<b>Late onset:</b>				
A.J	1	66	U	U

\* Body sites: U=upper face, F=lower face, J=jaw, T=tongue, P=pharynx, L=larynx, S=speech, swallowing, A=arm, K=arm, G=trunk, N=neck, H=hearing loss.  
 (no.=Number of individuals in group with that site affected.)

<sup>b</sup> Three of these individuals had all known AJ ancestors, one was 7/8 AJ, and one was 1/2 AJ.

<u>Sample number</u>	Genotype			
	D9S2160 <sup>a</sup>	D9S2161	D9S63	D9S2162
18843	3,4	2,2	8,8	4,4
13709	4,4	2,6	14,14	NT <sup>b</sup>
14122 <sup>c</sup>	3,3	4,4	0,0	5,5
13945	4,4	1,5	18,18	NT <sup>b</sup>
14040	2,5	1,2	16,16	2,4

<sup>a</sup> Markers listed from centromere to telomere: D9S2160 - <40 kb - D9S2161 - 150 kb - D9S63 - 130 kb - D9S2162 (Ozelius et al., 1997a).

<sup>b</sup> Position of DYT1 gene

<sup>c</sup> Not tested.

This individual had onset at 7 years in the arm with eventual involvement of the arm and neck and a positive family history of movement disorder (father with tremor). He was also apparently homozygous for markers D9S159-D9S2158-D9S2159, which are proximal to DS2160 (total region of 100 kb).

FIG. 11

FIG. 12A

Intron Primers Used to Amplify DYT1 Exons			
Exon	Primer Sequence (5' → 3')	SEQ. ID NO.:	Product Size (bp)*
1	GCAAAACAGGGCTTGTACCG	(SEQ. ID NO.: 30)	
	AGTAGAGACGCCGGTAGATG	(SEQ. ID NO.: 31)	
	GCGTCTCTACTGCCTCTTCG	(SEQ. ID NO.: 32)	
	ATGCCCTGGCCTAGTTAG	(SEQ. ID NO.: 33)	
2	GGTTTCGCAAGGTGCTTGG	(SEQ. ID NO.: 34)	408
	GGGATTCCAAACTTCCATCC	(SEQ. ID NO.: 35)	
3 and 4	TCCATGGGTTGGTAGGAAC	(SEQ. ID NO.: 36)	804
	GGTGACAGAGTAAAACATCTG	(SEQ. ID NO.: 37)	
5	GACCCCCAGTAGACGTTGT	(SEQ. ID NO.: 38)	640
	GTAAAAAAATCATGAGCCCTGC	(SEQ. ID NO.: 39)	

FIG. 12B

Intron Primers Used to Amplify TORB Exons			
Exon	Primer Sequence (5' → 3')	SEQ. ID NO.:	Product Size (bp)*
1	n.d. <sup>#</sup>		-
2	CCAGAGTTAGTGAGCAGGTC	(SEQ. ID NO.: 40)	526
	GAAGCGTTAAGGACCTCCAC	(SEQ. ID NO.: 41)	
3	ATCTATCTGCCAATTCCAC	(SEQ. ID NO.: 42)	466
	GTCCTGGTAAACAAAGTGCTG	(SEQ. ID NO.: 43)	
4	TGGGGTTACTCTATGTTGGTC	(SEQ. ID NO.: 44)	440
	CTAGCACAGTATGCCCTAAG	(SEQ. ID NO.: 45)	
5	TGAGGAATGTGCTGAGGGTC	(SEQ. ID NO.: 46)	333
	GCTGTCTCCTACCCATCTG	(SEQ. ID NO.: 47)	

\*PCR products were generated using oligonucleotides synthesized from intronic sequences, and accordingly the size of each product includes both intron and exon sequence.

#Not done. It was not possible to identify primers which could consistently PCR this exon.

<i>Protein</i>	<i>Organism</i>	<i>Gene</i>	<i>Locus</i>	<i>Accession</i>	<i>UniGene</i>
hTorsinA	human	DYT1	Chr.9, D9S159-D9S164	AF007871	Hs.19261
mTorsinA	mouse			AA230756	Mm.40438
rTorsinA	rat			AA850233	Rn.20041
sTorsinA	pig			AU058534	
hTorsinB	human	TORB	Chr.9, D9S159-D9S164	AF007872	Hs.5091
mTorsinB	mouse			AA596988	
drTorsinC	zebrafish			AA542632	
hTorp1	human	TORP1		AA873275	Hs.59038
mTorp1	mouse			AA981789	Mm.33875
rTorp1	rat			H31561	
hTorp2	human	TORP2		AA150869	Hs.26267
mTorp2	mouse			AA791729	
dmTorp3	fruitfly	EG:84H4.1	DMC84H4	AL031766	
ceTorp4A	nematode	F44G4.1	CEC18E9	P54073	
ceTorp4B	nematode	Y37A1B.12	CEY37A1B	AL023835	
ceTorp4C	nematode	Y37A1B.13	CEY37A1B	AL023835	

FIG. 13

INTRON 1 OF DYT1 GENE

FIG. 14A: Clone 1:  
23g14-2-7050.cDNA (Length: 283) SEQ ID NO.: 48

1   gttaggctggg gcgggggctg gaggctgggg ctggggctgg ggctgggcga  
51   tggcactagg **gctgaactag** **gaccaggcg**a tggagaatgg aggatggagg  
101   ccgggggatg gcaccagggc cgggctagga ctagggctgg agcggggcct  
151   gggggctggg gctgggcgt ggcactaggg cgggttgggg ctggggctgg  
201   ggctggggga tggagcgggg ccgggggctg ggggtggggc tgggggatcg  
251   actagggctg gnttaggacc aggccgttgg cat

Bold = primer 4 (reverse sequence) from FIG. 12A  
Underline = 5' splice sequence from Intron 1 FIG. 9A

FIG. 14B: Clone 2:  
Harvey7-23g14-2.cDNA (Length: 375) SEQ ID NO.: 49

1   ggatggtgga tggaggctgg gggatggcag tagggccggg ctaggactgg  
51   ggctggagcg gagttttgggg ctggggctca ggagcggggg ctggggctgg  
101   ggctggggct gggggatggc actaggcgag gccggggtag gggtcacatc  
151   ccaggaggcg cgggctgggc agagctgagt ccgcgggggc cggacccccgg  
201   aagccaagcn gccggcctgc aggatgagggc ctggctccctc ggccatgacc  
251   acagacgtgc cagacttaag tacggagacc tgaggagcca ggctgcagtt  
301   ggcctacttt ncncctaagct gggggtgtggac cagtggtaac ctccctccgaa  
351   gtgggttctg ctctttctag cctag

FIG. 14C: Clone 3:  
23g1-Harvey11.cDNA (Length: 439) SEQ ID NO.: 50

1   ccactgcccac tgccaccagt ttgcaccctt aaccctgtt ctgctccatcc  
51   caccckaagg cagagccggn gaaaggaaac agtttggtcc ctcctggtcc  
101   gctgcggaaag agtctcacca tccttctgtc tcccttagcta gaaaggaggc  
151   agaaccaca ttccggagggc ggttaccact ggtccaccc cagcttagcg  
201   caaagtaggc caacctgcac gcctggnnct cctcaggntc tgcctactta  
251   agtctggcag ctctnnntca tggccgaggt agccaggctc atccctgcagg  
301   nnccngccnn ttgnctncc ggggtntcgn nncccccgtac tcagctcgtc  
351   cagccggcct ctggatgtga cctaccgtc cttagtgcac ccagccagcc  
401   agccagccgt cttagccagcc aactgtctag ccagtctag

FIG. 14D: Clone 4:  
23g1-Harvey6.cDNA (Length: 378) SEQ ID NO.: 51

1   ctggaaaaga caaagccaat caggagtggg gaagaaaacac ggcaaaatgt  
51   agccacattt acagccata aganagccag caaagccgtc tagcctccaa  
101   *gcaccttgcg aaacctcaag tactgcggc* tggtaagctc ctggcccaga  
151   ggggacggcg gtccaggng ccctccctt gctggctctg cctattctaa  
201   *agccctggcc cgnctccctc* ccgaaaagcc ccttggtgcc actgccactg  
251   *ccaccanttt gncccccata ccctgtnc* tgcctccac cccaaaggcag  
301   *atgcggnnngg ngaaaggaaa cantttggc* cctcctggtc ggctcgngga  
351   *agactcctca ccatccttcc* tgtcttcc

Bold = primer 5 from FIG. 12A  
Italics = sequence overlap between Clone 4 and Clone 3  
Underline = 3' splice site from FIG. 9A

FIG. 14E: Clone 4:  
23g1-Harvey6.cDNA (Length: 388) SEQ ID NO.: 88

1   ctgggaaaaga ctgggaaaaga caaaagccaat caggagtggg gaagaaaacac  
51   ggcaaaaatgt agccacattt acagccata aganagccag caaagccgtc  
101   tagc**c**tccaa **gcac**c**t**tg**cg** aaac**c**tcaag tactgcggtc tggtaagctc  
151   ctggcccaga ggggacggcg gtccagggng cc**c**tcc**c**ttt gctgg**c**c**t**g  
201   c**c**tatt**c**taa agcc**c**tgg**c**c cgn**c**t**c**ttc cc**g**aaaag**g**cc c**t**ttgg**g**cc  
251   actg**g**cc**a**ct**g** ccacc**a**nt**ttt** gc**n**ccc**c**tac cc**c**tgt**n**ct**g** ct**c**c**t**cc**c**ac  
301   ccc**a**agg**g**cg atgcggnn**gg** ngaaaggaaa can**t**ttgg**t** c**t**c**c**tgg**t**cc  
351   gg**c**t**c**ng**g**ga agact**c**c**t**ca cc**a**t**c**c**t**cc t**g**t**c**tt**c**c

Bold = primer 5 from FIG. 12A

Italics = sequence overlap between Clone 4 and Clone 3

Underline = 3' splice site from FIG. 9A

INTRON 2 DYT1 GENE

FIG. 15A: Clone 1:  
29a5-6343.cDNA (Length: 400) SEQ ID NO.: 52

```
1      gaatatttac gagggtggtc tgaacagtga ctatgtccac ctgtttgtgg
51     ccacattgct ctttccacat gcttcaaaca tcaccttgc caaggcaagg
101    atggaagttt ggaatccctt cctggatgtc atcgggtttg gggctctttt
151    gttgtggat gagatttggg agttctatgt tgaaatgagt gagcccgaa
201    aacggttcat gtctcagttc cccttggaaa ggtgtagaag ttaagagttt
251    gagatgcgtg gagcagttaa taccatcaa gctttgtgg gggttctgaa
301    aatcgtcca gtgagttatgt agggtcatgg gatttttagag gtggacatga
351    tcaaattccat ctttagagatc aacacatctc actcattttt attttcttat
```

Bold = primer 6 from FIG. 12A

Underline = 5' splice site sequence for intron 2 from FIG. 9A

FIG. 15B: Clone 1:  
29a5-6343.cDNA (Length: 402) SEQ ID NO.: 89

```
1      gaatatttac gagggtggtc tgaacagtga ctatgtccac ctgtttgtgg
51     ccacattgct ctttccacat gcttcaaaca tcaccttgc caaggcaagg
101    atggaagttt ggaatccctt cctggatgtc atcgggtttg gggctctttt
151    gttgtggat gagatttggg agttctatgt tgaaatgagt gagcccgaa
201    aacggttcat gtctcagttc cccttggaaa ggtgtagaag ttaagagttt
251    gagatgcgtg gagcagttaa taccatcaa gctttgtgg gggttctgaa
301    aatcgtcca gtgagttatgt agggtcatgg gatttttagag gtggacatga
351    tcaaattccat ctttagagatc aacacatctc actcattttt attttcttat
401    tt
```

Bold = primer 6 from FIG. 12A

Underline = 5' splice site sequence for intron 2 from FIG. 9A

FIG. 15C: Clone 2:  
6550-54a5s.cDNA (Length: 418) SEQ ID NO.: 53

```
1      tttggagtga gacaggactg gggtcagggtc ccagctctgc cacatatagt
51     cttgggcaag tggagtaagc gctctctgtc cctcagttcc ctcatctgt
101    aaatgagaac gatagtgccc actccatggg gttggtagga acaaagaaga
151    ttttgggcat gtaaagttct tagtgcgcag tgcacagtgg tctgttaagt
201    aagctgcgtt tcttagtggt agaaggagct gattgatggc cctggctgag
251    aactttgtgt tcgccttttc ccnttttaat tcaggatcag ttacagttgt
301    ggattcgagg caacgtgagt gcctgtgcga ggtccatctt catatttgat
351    gaaatggata agatgcgtgc aggcctcata gatgccntca anccttcct
401    cgactattat gacctgg
```

Bold = primer 7 from FIG. 12a

Underline = 3' splice sequence for intron 2 from FIG. 9A

Italics = EXON 3 sequence

INTRON 3 DYT1

FIG. 16A: Clone 1:  
6202-54a5.cDNA (Length: 198) SEQ ID NO.: 54

```
1   ctcgactatt atgaccctggc ggatggggtc tcctaccaga aagccatgtt
51  catatttctc aggtaaggtc agggcttagga catgatggat gggccccgag
101 cccaaggcctc tgagctccag gaaaaaacc tgccttacc cactgggattttttgcagc
151 ttttgcagc aatgctggag cagaaaggat cacagatgtg tttggatt
```

FIG. 16B: Clone 1:  
6202-54a5.cDNA (Length: 200) SEQ ID NO.: 90

```
1   ctcgactatt atgaccctggc ggatggggtc tcctaccaga aagccatgtt
51  catatttctc aggtaaggtc agggcttagga catgatggat gggccccgag
101 cccaaggcctc tgagctccag gaaaaaacc tgccttacc cactgggattttttgcagc
151 ttttgcagc aatgctggag cagaaaggat cacagatgtg gctttggatt
```

**Bold** = EXON

Underline = sequence from for 5' splice site sequence and 3' splice site sequence, respectively from FIG. 9A

INTRON 4 DYT1

FIG. 17A: Clone 1:  
Intron 4-5 prime.cDNA (Length: 535) SEQ ID NO.: 55

1     **GTCTGTGTCG** GTTTCAATA ACAAGAACAG gTGAGTAGGG CCATCCACCG  
51    CCAGTCCCCT ATGGTTCTTA ATCCTGCACC CTAAGTGTAA AAAGCATCAG  
101   GGTCACTGTC AGCATCACCT GGGAGCTGGG TAGAAAGAAA TGgAGATTCT  
151   CAGTCCCCCTT CCGAGTCATG AGGGGAATCT TTGCTGATGA ACTCCAGGTA  
201   ACTTTTATGA ACACATAATGT TTGACAAGTG CTGTTTATT TTTATTTTC  
251   **AGATAGTTTT** **ACTCTGTCAC** CTAGGCTGGA GTGCAGTGGC GTAACCTTGC  
301   CTCACTGCAA CCTCTGCCTC CCGGGCTCAA GCGATTCTTG TGCCTCAGCC  
351   TCCTGAGTAG CTGGGATTAC AGGTGCACAC CATGCCAAG CNAATATTT  
401   GTATTTTAG TAGAGANGGG GCCCCGTNCA TGTTAACAG GCTGGTCTTG  
451   AACTNTTACC TCAGGTGAGT CCNCCACCTC GGCCCTCCAA AGTGCTGGGA  
501   TTACAGGCCT GAGCCACTGT GTCTCAGCTT ATTTTT

Italics = EXON sequence

Underline = 5' splice sequence from FIG. 9A

Bold = primer 8 from FIG. 12A

FIG. 17B: Clone 2:  
Intron 4-3 prime.cDNA (Length: 1302) SEQ ID NO.: 56

1     *GCCACTCCAA* GCTACCATCT GAGATTGTT CCTGCCCTAG AGTGGTAAAG  
51    *GCGTGAGGTC* CGTCTGCCCT CAGCTGTGTC CCCAGGCCA GGGCGTGCCT  
101   *GGCAACANNA* GCAGGCCTCT GAGAACACAGC CTCCCACGTG AGTTCATGAT  
151   *AGNAAGACAG* CCCCTCGTTC CCATTCACTG GTTGGTTCTG TTCTTYCCT  
201   *GGCMATAAGC* TCCACTCTGY MRTCAGCCAM ACATTTATTG AGTACCAAGTT  
251   *GTTGCCAAAG* CACTGTTGGG CATGAAAAGC ATTAACCCAG TGAATGAGGA  
301   *GGAGCTTGGG* TTGGGACGGA GCCMCARAAC TACATGGCAG ACCAGAAGGA  
351   *AATCAGCTCA* AGTAGAAARA CACGCATGGG CTCGTGGCG ACGCAGTGTG  
401   *TGCTGTGTC* TCTGGGCTG GGAGGAAGTG TCCTGGATCA GGAGTTCCAG  
451   *GAGGCCAGGA* GGAGTGGACG GGTCACTGCA GAGCCAGCCC GCAATCAGGG  
501   *GAAGAAAACA* CGGCCAAGGC CAGGCCTTCA CGGGGAGGCC AGCGTGGCT  
551   *GCACATCTGC* ACTCTCCAGG CTAGTTTGG TGCCCACATG CTCTGCAGGG  
601   *TCTGGCACT* GTGGCAGCGG CAGCAGGCCT CCCTGTTGCT AGTCCAGCTG  
651   *CTGAAACTCC* AGGGAGAGTC AAAAAGTTCC CAAATACAGA GGCAGTGGCTG  
701   *GTAGTCCTTC* CCGGGAATTC TTCTTGCTTC CCGCTTCTG TGGAACCTCTG  
751   *CCTTCCCCAC* TCTGCCTCTC TGCTTGTTC TGGGCCAG GACCTCTTC  
801   *CCATCTTCGA* TCTCTTAAGT CATACTTGG GAGGCCTCCC CCAGCCGCC  
851   *GTGTAAAGAG* GGCTGTACAC GCTTCTGCTG TCACAGAAGC ATTACAATGT  
901   *GCAGGTGCCT* GTTAACATCT GCCTTCCCCA CTGATCTGGA GCTCCACAAAG  
951   *GGAGAGGGCA* CACCCAGTAG GTATGTGTGG GATGGATAG AGGGTGGATG  
1001   *ACACCCAGTA* GATGTGTATG GGATGGATAG GAGGGTGGAT GACACCCAGT  
1051   *AGGTGTGTAT* GGGATGGATG GGAGGGTGGG TGACCCCTAG TAGATGTGGG  
1101   *GGGGTGGGT* GGGTGACCCC CAGTAGGTGT GTGTGGCATG GATAGGTGAC  
1151   *CCCCAGTACA* CGTTTGTGGG ACGGATGGGA GGGTAGGTAA GTGACCCCCA  
1201   *GGAGGCGTCT* ATAGGGCAGG TGGGTGGATG TGGATGAACA GCACCTTGT  
1251   *TCTTCTTCCC* AGGTGGCTTC TGGCACACAGCA GCTTAATTGA CCGGAACCTC  
1301   AT

Bold = primer 9 in FIG. 12A

Underline is 3' splice site sequence from FIG. 9A

Italics is EXON 5 sequence

INTRON 1 5' from TORB

FIG 18A: Clone 1:  
h59-29a5.se (Length: 240) SEQ ID NO.: 57

1 ggagcggccg ctcaacgctt cgggtacggc gcgcgcgcga gctgtgggtc  
51 ggcgcgtcgcc gggggcgccgg ggccgcgggg cgcggaggga cggcctcgta  
101 ggcgcctggc acggaccggg cccgtggcat ctagacggcg gtggtcccag  
151 ctgggggtggg cggggagcgg atggggcggc cccggaaccg ttcgcnggaa  
201 cgcagaagcn gtgcacttgaa acactctcag atcgtgnngc

INTRON 1 3' from TORB

FIG. 18B: Clone 2:  
5667s-29a5.Se (Length: 310) SEQ ID NO.: 58

1 gggaccaaag gacgtccgtc gttcccaccc accctaatcg ttgcgcngtc  
51 ngttcgctac ccagtagaga gacttactta cnngtnnacg gaaggaatag  
101 tctggggctt **cgcaattact** ggagggttat tagaactttc accgttagcaa  
151 actgacggag ccgggatccc acaccgcctg tgggnncgac acgggaccta  
201 ttgacacgaa gaacgaaacn gtcgatttt tcacgacgca acgactacgt  
251 aaaaattcca gacaaagaga gaaacaagac cccgacaaga acgtcGAGAG  
301 TTGACCTAA

Upper Case Letters = EXON (bottom strand)

Underline = sequence from Table 1

Bold = 2<sup>nd</sup> primer from FIG. 12B

INTRON 2 5' from TORB

FIG. 19A: Clone 1:  
6101-29a5.Se (Length: 401) SEQ ID NO.: 59

1 CAGGAACAAAC AAAAATCCCA AGAAACCCT GACCCTTTCC TTACACGGCT  
51 GGGCTGGCAC AGGCAAGAAT TTTGTCAGTN AAATTGTGGC TGAAAATCTT  
101 CACCCAAAAG GTCTGAAGAG TAACTTTGTC CACCTGTTG TATCGACTCT  
151 GCACTTCCT CATGAGCAGA AGATAAAAAGT ACCAGGgca agagaacccg  
201 ctattatctc gtctgcaggc cagtcggact ggtccgggtg **acctgctcac**  
251 **taactctggc** ctctgcttct ctttcctttg tggtgctgta gccccccggct  
301 ccactgagtt aaggcacact tagtccaggt agttacaaaag ctctcctaca  
351 acatttctta cttgggttcca aaacagtcca gtggggtagg ggatgttatt  
401 t

Upper Case Letters = EXON  
Underline = 5' splice site sequence from FIG. 9B  
Bold = 1<sup>st</sup> primer from FIG. 12B

INTRON 2 3' TORB

FIG. 19B: Clone 2:  
29A5-39-11.se (Length: 238) SEQ ID NO.: 60

1 ttctgttaact ggtcCTGGAC CAACCCATGAA AGAAGAAACA GGATGCGAAG  
51 CTCAAAGGGC TGCAACCAAGA GGCAGCGCAGG CTCCATCTGC TCCTCATGCA  
101 CTGAAGGACG AGGTCAAGAGC TCTTAGAATG GCACCCCTCAC CCCCACTCGC  
151 TAGGTAGCAG CTTTCTAAA ACCTTATCTC TAAAAAGTGG **AAATTGGCAG**  
201 **AGATAGATGC** TAAAATGCAG AGAAGTTTT CCTAACTC

Lower Case Letters = EXON  
Underline = sequence from Table 1  
Bold = primer 3 from FIG. 12B

INTRON 3 5' TORB

FIG. 20A: Clone 1:  
39-14-29a5.Se (Length: 391) SEQ ID NO.: 61

1     GGGATCATTG ACGCAATCAA GCCGTTCTA GACTACTACG AGCAGGTTGA  
51    CGGAGTGTCT TACCGCAAAG CCATCTTCAT CTTTCTCAGg tcagcggag  
101   gcggttttt gggcacaca agcccttcat tctctcaatg ataaaatgag  
151   gtcctgagga ccat**cagcac** **tttgtttacc** **aggac**gaaag tgccctgcttg  
201   gcacaaggca cttacctact gctttacttt tcctttgccca gtcatcagca  
251   tggcacacag tgtgggttgt ggaaatgaac taaagaaata atcactggga  
301   caggcgcggt ggctcacacc tgtcaatccn agcactttgg gnaggcatgg  
351   cgggcggatc acaggagatc gagacatctg ctaacatgnt g

Upper Case Letters = EXON  
Underline = 5' splice site sequence from FIG. 9B  
Bold = primer 4 from FIG. 12B

INTRON 3 3' TORB

FIG. 20B: Clone 2:  
5665s-54a5.Se (Length: 373) SEQ ID NO.: 62

1     gtaagacaca gagtctttt tnttttttag accgagtnnc attnttgttg  
51    ccnanngctgg agtgcaatgg catgatctcg gctcgctgca acctccaccc  
101   cccggrrttca aacgattctc ccacctcagc ctccccatgta gctgggattta  
151   cagnatgca ccaccattag cctggctaatttttggttttttttagtagaga  
201   **tggggttact** **ctatgttgtt** caggctggcc ttgaactccc gacccctagg  
251   gatctacctg cctcggcctc ccaaagtgtt gggattacag ccatgagcna  
301   ccacnsnan cagacncaga agtcttaata tgtgattttt atcttttattt  
351   ctctgcaaaa ctcagCAATG CAG

Upper Case Letters = EXON  
Underline = 3' splice site sequence from FIG. 9B  
Bold = primer 5 from FIG. 12B

INTRON 4 TORB

FIG. 21: Clone 1:  
intron4torb.se (Length: 310) SEQ ID NO.: 63

1     gtgagtccac cagggtaaaag gagcccccta actgtccagc agtgagccgt  
51    ctgctctttc attgagtgtt tgcacaaagc cacaggatcc cactggattt  
101   cctcactttg ctaaagtcaag gaattttctt **agggcatact** **gtgctagaaa**  
151   ccagttagtg agtgtccagc tgagtccctcg atgggcttgc tgcacactga  
201   caagagacnc tctcaagggg tacggacatg **aggaatgtgc** **tgagggtcgg**  
251   gactggagct tggccaggtg gcggtggtgg cagggaaaccc agctgtgtct  
301   tgttctgcag

Underline = 5' splice site sequence from FIG. 9B

Bold = primer 6 from FIG. 12B

Underline italics = 3' splice site sequence from FIG. 9B

Bold italics = primer 7 from FIG. 12B

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